REMARKS

The Final Office Action of November 25, 2009, and the Advisory Action of February 24, 2010, have been received and reviewed. Please amend the specification and claims as previously set forth in conjunction with the Request for Continued Examination filed herewith. All amendments and claim cancellations are made without prejudice or disclaimer. No new matter has been presented. Reconsideration is respectfully requested.

Interview

The applicants' representative would like to thank the Examiner for the courtesy extended them during the phone interview of March 22, 2010. The interview was very helpful to the applicants and their representative in gaining an understanding of the Examiner's concerns. In the interview, basis for the amendments presented herein were discussed as were the Examiner's and applicants perspectives with respect to the amendments. As discussed at the interview, applicants are amending the application as previously set forth in an effort to remove outstanding issues and otherwise expedite prosecution. If the Office believes that further comments are necessary or desired describing the interview, the Examiner is kindly requested to contact applicants' undersigned attorney, and further detail will be promptly provided.

Sequence Compliance

In addition, applicants have amended ¶¶ **[0011]**, **[0012]**, **[0021]**, and **[0044]** of the Specification to further recite the proper sequence identifiers. ¶ **[0047]** has been amended to recite Gln in place of Glu to be consistent with FIG. 1 and SEQ ID NOS: 6 and 7. Consequently applicants submit that the application is in compliance with 37 C.F.R. §§ 1.821-1.825. Withdrawal of the objection to the Specification is respectfully requested.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 27-30, 47, and 49 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Claims 27 and 47 assertedly omit the essential step of translating the expressed nucleotide. Final Office Action of November 25, 2009, at page 4.

Although applicants do not agree that any of the claims are indefinite, to expedite prosecution, claims 27 and 47 have been amended herein to recite translation of the expressed nucleotide. Consequently, applicants respectfully request withdrawal of the rejections of claims 27-30 and 47 under 35 U.S.C. § 112, second paragraph, and reconsideration of same.

Further, claim 49 stands rejected as assertedly being indefinite for the use of the term "or" in lines 5, 7, 8, and 9. *Id.*

Although applicants do not agree that any of the claims are indefinite, to expedite prosecution, claim 49 been amended herein to no longer recite the term "or" at the specified locations. Consequently, applicants respectfully request withdrawal of the rejection of claims 49 under 35 U.S.C. § 112, second paragraph, and reconsideration of same.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1-4, 8-10, 27-30, and 46-48 stand rejected under 35 U.S.C. § 112, first paragraph, for assertedly failing to comply with the written description requirement. Applicants note that the rejections of claims 2 and 4 are moot as those claims have been cancelled herein. Applicants have amended claims 1, 27, and 46-48, and partially in view of those amendments, respectfully traverse the remaining rejections as hereinafter set forth.

Applicants respectfully note that a sequence can meet the written description requirement under *Enzo Biochem, Inc. v. Gen-Probe Inc.* through the showing "relevant identifying characteristics *i.e.* complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. 296 F.3d 1316, 1324 (Fed. Cir. 2002) (emphasis added). Applicants respectfully note that added emphasis on "or" which applicants submit clearly indicates that one does not have to meet each and every one of the test outlined by the *Enzo* court, but that any one of them can be met to satisfy the written description requirement.

Applicants further note that the genus of "variants" can also be provided with adequate written description "through sufficient description of a representative number of species by actual reduction to practice." M.P.E.P. § 2163(II)(A)(3)(a)(ii) Further "what constitutes a 'representative number' is an inverse function of the skill and knowledge in the art." *Id.* Applicants respectfully submit that the skill and knowledge concerning nucleotides sequences in

the biotechnological arts is very high.

Applicants further submit that one of ordinary skill in the arts would readily conclude that the applicants were in possession of a common attribute possessed by members of the genus; . . . *See, e.g.*, M.P.E.P. § 2163(II)(A)(3)(a)(ii)

Although applicants do not agree that any of the claims lack written description, to expedite prosecution, the claims have been amended herein. Specifically, the claims have been amended to recite that the at least one glycosylation site that has been removed is an N-glycosylation site.

The Office states, on page 7 of the Final Office Action of November 25, 2009, that while the applicants are in possession of SEQE ID NO:7 and the designated fragments thereof, the applicants do not show possession of species which require "unknown modifications" to the amino acid SEQ ID NO:7. Specifically the Office asserts that the determination of which potential amino acid sequence modification that would be encompassed by the claims requiring removal of glycosylation sites and correlate to the production of properly folded proteins would not be predictably. Applicants respectfully disagree.

The presently claimed methods provide AMA-1 ectodomains or designated fragments thereof that have been modified to remove at least one N-glycosylation site. Furthermore, mAb 4G2 exhibits specificity for said ectodomains or fragments. As described at ¶ **[0015]** of the Specfication, AMA-1 contains six N-glycosylation sites that are potentially recognized by eukaryotic systems. A person of ordinary skill in the art at the time of the invention would have been aware of the N-glycosylation consensus sequence. The application further describes in the same paragraph how at least one of the six sites may be removed. The claims therefore define sequences that can be predictably modified at six sites to remove at least one N-glycosylation site.

As noted by the Office, a genus can be adequately described if the disclosure presents a sufficient number of representative species. Description of a representative number of species does not require that the description to be of such specificity that it would provide individual support for each species that the genus embraces, and what constitutes a "representative number" is an inverse function of the skill and knowledge in the art. M.P.E.P. § 2163 (II)(A)(3)(a); In re Bell, 991 F.2d 781, 785 (Fed. Cir. 1993); In re Baird, 16 F.3d 380, 382 (Fed. Cir. 1994).

Applicants have provided working examples for the removal of all six potential glycosylation sites (*see, e.g.*, ¶ **[0047]**). Applicants have further shown that modification of these six sites results in an AMA-1 ectodomain that is properly folded and can react with mAb 4G2 (*see, e.g.*, ¶ **[0051]**). A person of ordinary skill in the art, at the time of the invention, would thus have concluded that none of the potential N-glycosylation sites is required for proper folding and that these sites can be modified without affecting the conformation or the ability to react with mAb 4G2.

Satisfactory disclosure of a "representative number" depends on whether one of ordinary skill in the art at the time of the invention would have recognized that the applicants were in possession of the necessary common attributes or features of the element possessed by the members of the genus in view of the species disclosed. *See, e.g,* Eli Lilly. As applicants have successfully modified all six potential N-glycosylation sites, a person of ordinary skill in the art at the time of the invention would have necessarily recognized that the applicants were in possession of a representative number of species.

In the previous response of the applicants, several arguments were made regarding the Fandeur reference cited by the Office in the Office Action of April 1, 2009, namely that Fandeur provides no suggestion of unpredictability in AMA-1 variants or in producing properly folding protein and that Fandeur suggests that while there may be some different effects by the strains, there is predictability that transcends strain diversity. The Office has stated in the present Final Office Action that applicants arguments are not found persuasive, however the Office has failed to state the reasons for this decision (*see* 37 C.F.R. § 1.113). Fandeur describes *Plasmodium* variants that differ from each other in a number of characteristics (*see* bridging paragraph 225-226). Fandeur however, is silent regarding AMA-1 and fails to suggest unpredictably of the claimed subject matter.

The Office states that the claims require experimentation to determine which modified nucleic acids would encode polypeptides that would be folded correctly. Applicants fail to understand the relevance of this statement in the determination of compliance with the written description requirement. Nevertheless, any experimentation required by a skilled person to practice the claimed invention is merely routing, is guided by the specification, and is not an undue burden.

The Office further asserts that the claims use the open language "comprising" and as such do not expressly limit the ectodomain. The disclosure teaches one of skill in the art that the AMA-1 ectodomains that are necessary for reactivity with mAb 4G2, namely domain I or domains I + II. This domain(s) is required for reactivity, however, and nothing in the disclosure or the art suggest that additional sequences would interfere with proper folding of the protein. As one example, Table 2 demonstrates that antigen Pf 11-0 having AMA-1 residues 25-545 is properly folded. Therefore, ectodomain fragments such as 97-442, can clearly encompass additional amino acids and still fold properly. However, in an effort to expedite prosecution, the claims have been amended to recite fragments consisting of the particular amino acid sequences.

Furthermore, the Office states that claim 49 does not refer to any specific amino acid fragment. Claim 49 is amended herein to refer to amino acids 97-442 of SEQ ID NO:7. The Office also states that the claims are directed to nucleic acids and not to polypeptide fragments. The claims are amended herein to refer to the amino acid sequence of the ectodomain and the fragments.

An objective standard for determining compliance with the written description requirement is: "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989). The disclosure provides working examples of AMA-1 ectodomain and fragments that have been modified 1) to remove all six potential N-glycosylation sites and 2) to utilize the yeast cell's codon usage. The working examples demonstrate good protein expression, proper folding, and are reactive to mAb 4G2.

In view of at least the foregoing, applicants respectfully submit that one of ordinary skill in the art at the time of the invention would have reasonably concluded that applicants possessed the claimed subject matter. Applicants further submit that this conclusion is buttressed by the level of skill and knowledge of art at the time of the invention and the representative number of species disclosed in supporting the scope of the claims. Consequently, applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, and reconsideration of the claims.

CONCLUSION

In light of the above amendments and remarks, applicants respectfully request reconsideration of the application. If questions remain after consideration of the foregoing, or if the Office should determine that there are additional issues which might be resolved by a telephone conference, the Office is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

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Date: March 22, 2010